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Kinetics and intracellular compartmentalization of HTLV-1 gene expression

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Human T cell leukemia virus Type 1 (HTLV-1) codes for at least 9 alternatively-spliced transcripts and two major regulatory proteins named Tax and Rex that function at the transcriptional and post-transcriptional levels, respectively. We investigated the temporal sequence of HTLV-1 gene expression in primary cells from infected patients using splice site-specific quantitative RT-PCR. The results indicated a two-phase kinetics with the Tax/Rex mRNA preceding expression of other viral transcripts. Using transfection of HTLV-1 molecular clones and subcellular RNA fractionation we demonstrated the Rex-dependency of the two-phase kinetics and determined the compartmentalization of the individual mRNAs, showing that over 90% of the HBZ mRNAs were retained in the nucleus. Mathematical modelling revealed the importance of a functional delay of Rex function compared to Tax, which was supported by experimental evidence of delayed accumulation and longer half-life of Rex. These data provided the first evidence for a temporal pattern of HTLV-1 expression and revealed major differences in the intracellular compartmentalization of HTLV-1 transcripts.

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